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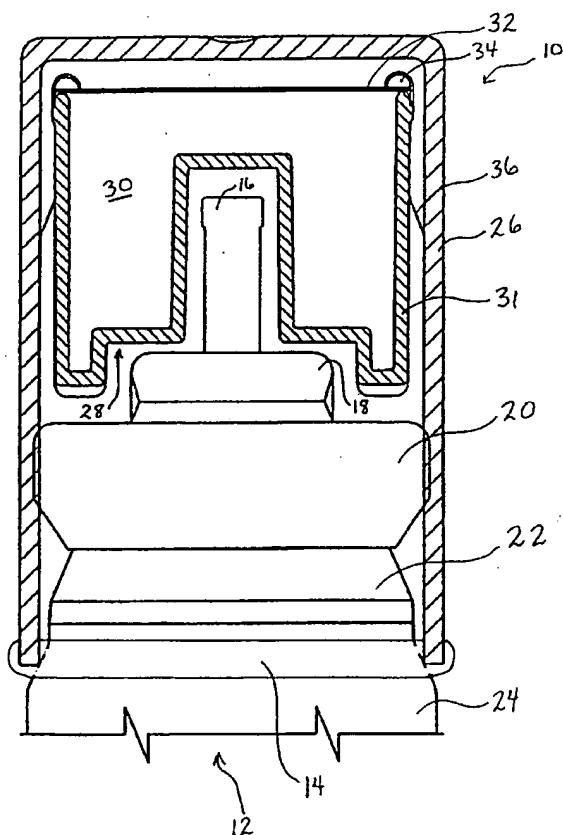
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- (72) Inventors; and
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- (30) Priority Data: 60/204,252 15 May 2000 (15.05.2000) US
- (74) Agents: **LEVY, David, J. et al.**; GlaxoSmithKline, Corporate Intellectual Property, Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,

[Continued on next page]

(54) Title: AEROSOL MDI OVERCAP CONTAINING DESICCANT



(57) Abstract: The subject matter relates to an overcap (10) containing a desiccant (30) for use with a metered dose inhaler (12) to adsorb moisture. The overcap advantageously reduces the amount and rate of moisture ingress into the metered dose inhaler. The operation of metered dose inhalers containing agrosopic drug particles is improved by reducing moisture ingress.



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(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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AEROSOL MDI OVERCAP CONTAINING DESICCANT

Cross Reference to Related Applications

U.S. Application having serial no. 60/204,252 filed on May 15, 2000, entitled "Method and Package for Storing A Pressurized Container Containing A Drug" is hereby incorporated herein by reference in its entirety.

Background of the Invention

As discussed in the above-referenced application, moisture ingress into HFC MDI's is problematic, particularly for MDI's containing hygroscopic drug particles which readily adsorb and/or absorb water and form aggregates. One solution to the problem has been to incorporate a desiccant to absorb moisture that in its absence would ingress into the MDI. The manner in which the desiccant is employed can, however, impact to varying degrees several factors.

For example, the structures employed for the desiccant can affect the cost of manufacturing. Complex and difficult mechanisms may reduce throughput, decrease efficiencies, and increase material costs. The form of desiccant packaging can also affect the visual and commercial appeal of the MDI. For example, to some vendors and customers, an internal, unseen desiccant may be more appealing than the overwrap and loose desiccant pouch disclosed in the above-referenced application.

Moreover, there is a strong need for effective prevention of moisture ingress in HFC propellant MDI's. It is well established that non-CFC propellants, especially HFC 134a, have much greater water solubility than the CFC propellants traditionally used in MDI's. The maximum water solubility in HFC 134a is about 2200 ppm (and about 1000 ppm in pressurized/stored MDI's) compared to about 130 ppm (and 50-100 ppm in pressurized/stored MDI's) for CFC 11, 12 and 114. The maximum solubility may be further increased where co-solvents such as ethanol are employed in the aerosol formulation. The mechanism of moisture ingress into HFC MDI's may be found in Williams, G. and Tcherevatchenkoff, A. (1999), "Moisture Transport Into CFC-Free MDI's," Respiratory Drug Delivery VI, Hilton Head, SC, USA.

They concluded that moisture ingress is influenced by the elastomeric nature of the valve gaskets as well as the type of HFA formulation and storage conditions employed. It may be appropriate under some circumstances to control moisture ingress into HFC-based MDI's. One example is where hygroscopic drug substance are used, such as albuterol sulfate.

The present invention advantageously reduces moisture ingress into MDI's to suitable levels. The present invention employs a desiccant in a manner that is visually appealing and commercially advantageous. The design and structure of the present invention is also advantageously simple, efficient to manufacture, cost effective, smaller and less bulky than other secondary packaging systems.

Summary of the Invention

One aspect of the invention is an overcap including an outer housing fitted with a moisture absorber structure having a housing containing a desiccant. The housing of the absorber is preferably constructed from a radially oriented material connected to a moisture permeable material. The radially oriented material is preferably an injection moldable plastic. The moisture permeable material is preferably fiberboard or TYVEK™ available from DuPont.

Preferably, the moisture permeable material is connected to the radially oriented material by crimping over a portion of the radially oriented material. The injection moldable plastic is preferably a polypropylene. The desiccant preferably includes a granular silica gel, preferably 2-10 grams.

In another aspect of the invention, the housing of the absorber includes at least one radially oriented fin. The radially oriented fin may be a circumferential fin. The absorber may also include a plurality of circumferential fins or a combination of radial and circumferential fins. The outer housing is preferably constructed from an injection moldable plastic, and more preferably a polypropylene.

In another aspect of the invention, the overcap is connected to a metered dose inhaler by a sealant. The sealant is preferably constructed from an epoxy material, such as DEVCON 2-TON EPOXY™. Preferably, the overcap and sealant seals off a valve stem, ferrule, valve housing and neck of the metered dose inhaler. The sealant is preferably a foil label. The foil label may be a structural laminate including an oriented polyamide layer, an aluminum foil layer and a pressure sensitive adhesive. The foil label preferably has a thickness in the range of 9-20 μm . The sealant may provide a hermetic seal between the metered dose inhaler and the outer housing. The metered dose inhaler may contain a drug such as albuterol sulfate.

Brief Description of the Drawing

The present invention will become more fully understood from the detailed description herein and the accompanying drawing which are provided by way of illustration only and are not to be construed as limiting the full scope of the invention.

Fig. 1 is a cross-sectional, cut-away view of the overcap of the present invention in combination with a portion of the metered dose inhaler.

Detailed Description of the Preferred Embodiments of the Invention

Shown in Fig. 1 is a cross-sectional, cut-away view of an overcap 10 connected to a portion of an MDI 12. The overcap 10 is connected to the MDI 12 by a sealant 14. The portion of the MDI 12 shown in Fig. 1 includes a stem 16, a ferrule 18, a valve housing 20, a neck assembly 22 and a cannister 24.

The overcap 10 includes an outer housing 26 fitted with a desiccant container 28 containing a desiccant 30. The desiccant container 28 includes a fitment housing 31 connected to a moisture-permeable overlay 32 to contain the desiccant 30. The fitment 31 is connected to the overlay 32 by a crimp 34 in the fitment 31. The fitment 31 also includes a radial fin 36 for friction fitting the desiccant container 28 within the outer housing 26.

An MDI containing albuterol sulfate and HFC 134a propellant was evaluated for moisture ingress using the overcap of the present invention. The sealant was DEVCON 2-TON EPOXY™; the injection moldable plastic was polypropylene, the desiccant was 10 g silica gel, and the overlay material was fiberboard. The results are shown in Table 1. The numerical values are the mean moisture content (ppm) of the MDI contents after storage at 40°C and 85% RH. The overcap was compared to a conventional shrink wrap seal and adhesive band seal.

Table 1

System	Initial	6 weeks	3 months
Epoxy Seal	204	280	232
Shrink Wrap	204	266	371
Adhesive Band	204	383	281

As the data demonstrates, the overcap was exceptionally effective at reducing the rate of moisture ingress into the MDI.

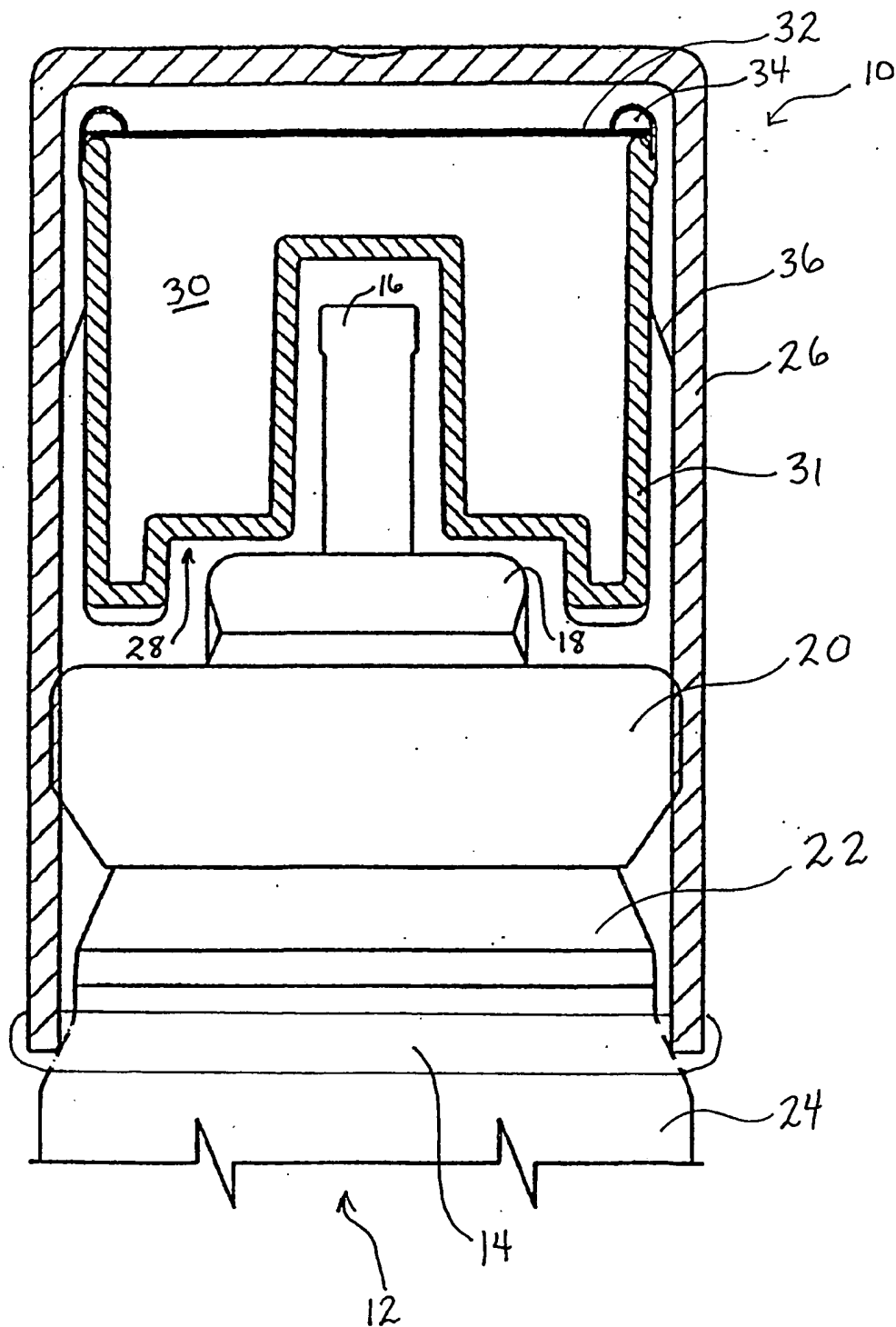
What is claimed:

1. An apparatus comprising: a first housing fitted with a moisture absorber comprising a second housing containing a desiccant.
2. The apparatus of claim 1 wherein the second housing is constructed from a radially oriented material connected to a moisture permeable material.
3. The apparatus of claim 2 wherein the radially oriented material is an injection moldable plastic.
4. The apparatus of claim 2 wherein the moisture permeable material is fiberboard.
5. The apparatus of claim 2 wherein the moisture permeable material is TYVEK™.
6. The apparatus of claim 2 wherein the moisture permeable material is connected to the radially oriented material by crimping over a portion of the radially oriented material.
7. The apparatus of claim 3 wherein the injection moldable plastic is a polypropylene.
8. The apparatus of claim 1 wherein the desiccant comprises granular silica gel.
9. The apparatus of claim 2 wherein the second housing includes at least one radially oriented fin.
10. The apparatus of claim 9 wherein the radially oriented fin is a circumferential fin.
11. The apparatus of claim 10 comprising a plurality of circumferential fins.
12. The apparatus of claim 1 wherein the first housing is constructed from an injection moldable plastic.
13. The apparatus of claim 12 wherein the injection moldable plastic is a polypropylene.

14. The apparatus of claim 1 further comprising a metered dose inhaler connected to the first housing by a sealant.
15. The apparatus of claim 14 wherein the sealant is constructed from an epoxy material.
16. The apparatus of claim 14 wherein a valve stem, ferrule, valve housing and neck are contained and sealed withing the first housing.
17. The apparatus of claim 14 wherein the sealant is a foil label.
18. The apparatus of claim 17 wherein the foil label is a structural laminate comprising an oriented ployamide layer, an aluminum foil layer and a pressure sensitive adhesive.
19. The apparatus of claim 18 wherein the foil label has a thickness in the range of 9-20 μm .
20. The apparatus of claim 14 wherein the sealant provides a hermetic seal between the metered dose inhaler and the first housing.
21. The apparatus of claim 8 comprising 2-10 g granular silica gel.
22. The apparatus of claim 14 wherein the metered dose inhaler contains albuterol sulfate.
23. An overcap for an aerosol container comprising:
a first housing fitted with
a means for absorbing moisture.

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Figure 1



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(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

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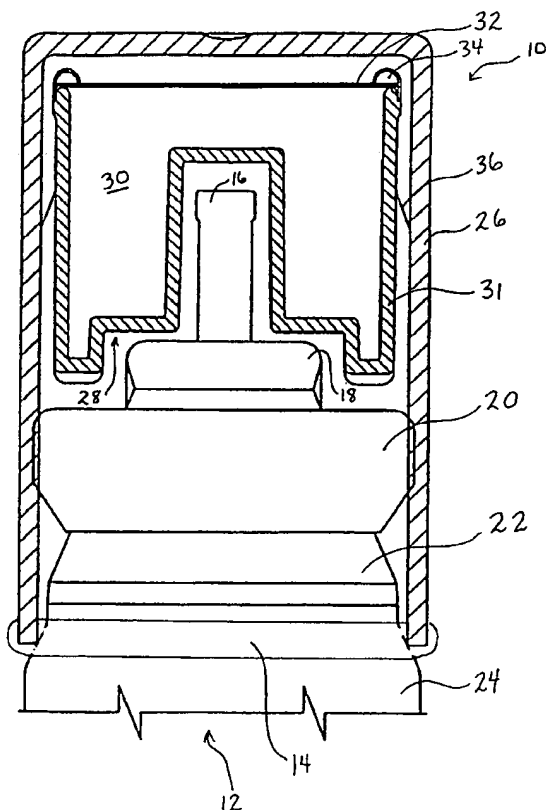
(75) Inventors/Applicants (for US only): **HERMAN, Craig, Steven** [US/US]; GlaxoSmithKline, Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US). **PISCULLI, Vincent, P., Jr** [US/US]; GlaxoSmithKline, Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US). **HAAN, Richard, J.** [US/US]; GlaxoSmithKline, Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US).

(74) Agents: **LEVY, David, J.** et al.; GlaxoSmithKline, Corporate Intellectual Property, Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709 (US).

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(54) Title: AEROSOL MDI OVERCAP CONTAINING DESICCANT



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INTERNATIONAL SEARCH REPORT

Intern Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 B65D51/30 B65D83/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 B65D A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 186 775 A (INCORVIA SAMUEL A ET AL) 16 February 1993 (1993-02-16)	1-3,5,8
Y	column 2, line 55 -column 3, line 52	4,6,7, 12,13
A	column 4, line 5-15; figures 8-12	21
X	US 5 749 496 A (DEJONGE SR STUART ET AL) 12 May 1998 (1998-05-12)	1,23
	column 3, line 66 -column 4, line 7; figures 1-3,6	
Y	DE 19 62 685 U (SANNER KG FRIEDR) 22 June 1967 (1967-06-22)	4,6
A	page 6, paragraph 1; figure 2	12,21
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- *8* document member of the same patent family

Date of the actual completion of the international search

4 February 2002

Date of mailing of the international search report

15/02/2002

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Intern Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 834 234 A (SACHERER KLAUS-DIETER ET AL) 30 May 1989 (1989-05-30)	7,12,13
A	column 3, line 16-51; figure 1	4,6,9, 10,21
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/15551

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-13,21,23

Subject I relates to an apparatus comprising a first housing fitted with a second housing containing a desiccant whereby the second housing is connected to a moisture permeable material.

2. Claims: 14-20,22

Subject II relates to an apparatus comprising a first housing fitted with a second housing containing a desiccant whereby a metered dose inhaler is connected to the first housing by a sealant.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern

Application No

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